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Some Notes on the "Parathyroid Duct" and its Relation to the Hassall's Corpuscles of the Thymus.

by

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A curious structure of a cystic nature has been observed by many investigators from the time of Sandström onwards in the parathyroid and thyroid glands of man and some of the lower animals. A similar tubular structure has also been noted in some instances in the thymus. The purpose of these notes is to give a detailed account of this structure as it is seen in the thyroid, parathyroid and thymus glands of cats and dogs, and to point out its apparent connection with the Hassall's corpuscles of the thymus. In the cat the connection between the various structures arising

arising from the gill clefts seems to be a particularly close one. Thymus modules are found almost invariably around, and occasionally in the centre of, the thyroid - parathyroid nodes are found in the thymus, and the cystic structure referred to is found in parathyroids, thyroid and thymus. This animal then affords very good material for the study of the relationships of these different organs.

Pepere[I] (Arch.Ital.de Biologie, 48 and 49), who made long and careful investigations into the structure and functions of the parathyroid glands, had named the structure I am about to describe, the "parathyroid duct", and this term I shall adopt for the same of clearness, though there is no evidence to show that it has any duct functions. In a series of 33 cat thyroids examined in serial section the "parathyroid duct" was found to be present in all, and thymic nodules in 27 cases.

The

The tissues examined were removed by Prof.Noël Paton and Dr.Leonard Findlay in the course of an investigation into the relationship of the parathyroid glands to tetany (Q.J.of Exp.Phys. 10. 1917). They were placed at once in picro-formalin - embedded in paraffin and stained with haemalum and eosin.

The appearance of the duct varied much in different instances, but I shall give first a general description of the type most frequently observed and then a more detailed account of the structure as seen in one or two different instances.

Very often the duct was observed first in the thyroid - most frequently perhaps about the centre, and it had almost the appearance of a specially large and thin-walled thyroid vesicle. Almost always, however, such a vesicle contained

contained a peculiar blue black homogeneous material, quite different from the pink stained colloid of the true thyroid vesicles, that made it easily recognisable. In some instances, in the progressive examination of serial sections the single seeming vesicle was observed to become gradually larger and to be broken up by septa until it had the appearance of a large cyst-like structure. At the same time an island, or islands of parathyroid tissue appeared beside the duct - these gradually surrounded it or coalesced alongside it.

Sometimes, as the parathyroid increased in size, the duct diminished and disappeared - sometimes it persisted as a large structure throughout all the sections containing parathyroid tissue and could be traced for some distance in the thyroid after the parathyroid had disappeared.

One

One of the most remarkable features of the duct was the variety of forms taken by the epithelium lining its walls. Sometimes - most often perhaps - it had the large loculated vesicular appearance already described, its thin walls lined by a single layer of very flattened epithelium. In other instances the epithelium lining the walls was columnar, long or short, and occasionally it was ciliated. Again, the lining of the walls was thick and composed of several layers of horny-looking, flattened epithelium.

Sometimes the lumen of the duct was almost or completely filled with epithelium of this nature, but less flattened.

In all the series of sections epithelium of this type could be seen in the duct channels breaking down and becoming necrotic. The duct was found rather more often in connection

connection with the internal than with the external parathyroid, but it appeared in or alongside either or both.

It's connection with the thymus nodules which are almost invariably found in the fibrous tissue capsule of cat thyroids, was also close and some very peculiar formations of mixed epithelial and lymphoid tissue were found within these thymus nodes or lying alongside them.

The following descriptions of the structure as seen in three of the cat thyroids examined will give an idea of the varied and peculiar forms it takes.

Cat 15.

In this animal the duct was first observed near the centre of the thyroid in the midst of a patch of tissue composed of small irregular thyroid vesicles, groups of very dark staining spindle and lymphoid cells, and one or two little solid clusters of epithelial cells with large rounded nuclei and rather indefinite pink staining protoplasmic bodies. It consisted at first of a small channel lined with rather tall columnar epithelium. This channel gradually increased in size and at one point the epithelial cells lining a portion of it were very tall and showed cilia.

Meantime other duct channels had formed by the breaking down of some of the little groups of epithelial cells mentioned above. Some of these persisted only for a few sections - others became large and loculated, with thin walls

walls lined with very flattened epithelium. Ultimately the appearance presented by the duct structure was that of a large loculated cyst-like structure, lying in a mass of tissue more compact than the ordinary thyroid tissue and composed of (1) small rounded or spindle-shaped cells whose nuclei stained very darkly with haemalum, and whose cell bodies could not be distinguished, (2) epithelial cells with rounded or oval nuclei of medium size and pink staining protoplasmic bodies, (3) epithelial cells with large oval granular nuclei,- the cell bodies of these were scarcely visible, (4) epithelial cells with rounded globular bodies apparently distintegrating and nuclei eccentrically placed. 3 and 4 were seen within the duct channels along with a great deal of rather granular homogeneous pink staining debris. Plate I. Figs. 1, 2, 3, 4, 5.

A few sections further on in the series definite parathyroid tissue (internal parathyroid) appeared alongside this

this mass of varied cells and duct loculi. The external parathyroid also appeared in the fibrous capsule of the thyroid. As the internal parathyroid increased in size the duct channels gradually decreased and finally disappeared. The lymphoid and spindle celled tissue was also gradually replaced by parathyroid or by normal thyroid tissue.

In the meantime small nodes of mixed lymphoid tissue and epithelial cells appeared and disappeared in a connective tissue reticulum close to the external parathyroid. The epithelial cells in these, which were in little groups or islets, broke down and formed small duct channels which persisted throughout a few sections and gradually disappeared, being filled up or encroached upon by the surrounding spindle or round cells of the nodes. Plate II. Fig.1, 2, 3, 4.

There

There was nothing of note in the formation of the duct channels in the other side of the thyroid in this animal.

In Cat 35 large duct channels formed in a patch of mixed lymphoid and spindle celled and epithelial tissue in the centre of the thyroid near the internal parathyroid in just the same way as in Cat 15. Plate 3, Figs. 1 and 2. whilst at the side of the thyroid in a piece of rather dense fibrous tissue in which lay also the external parathyroid the formation of duct channels by the breaking down of large epithelial cells in lymphoid nodes, conversion of the broken down epithelium into a homogeneous mass of necrotic material, the gradual disappearance of the ducts, and their ending, as they began, in small lymphoid nodes, after a course of about 24 sections was very well illustrated. Plate

Plate 3, Figs 3, 4, 5 & 6.

In Cat 39 duct channels formed as in the two previous examples, but in this animal the various stages of degeneration gone through by the epithelial cells in process of necrosis, and the peculiar longitudinal splits that are frequently seen in a degenerating mass of epithelium filling a duct channel were particularly well shown, Plate 4, Figs. 1 and 2. In one of the duct channels in this animal a certain amount of organisation of a partially necrosed epithelial mass filling a duct channel had apparently taken place as it contained small blood vessels.

These three animals illustrate the appearance of the duct channels in both lymphoid and epithelial tissue - the remarkable variety of cells of which their walls may be composed - the short extent of many of them and their apparently

apparently blind termination.

One may see a channel beginning by the breaking down of epithelial cells, becoming quite clear and distinct with a smooth regular lining of one layer of very thin flattened epithelial cells - gradually filling up again, or rather becoming encroached upon by the surrounding tissue and ending as it began in a little node of epithelial, lymphoid and spindle cells, all within the space of some half dozen sections.

Although the duct itself is apparently formed by the breaking down of epithelial cells, lymphoid and spindle cells almost invariably accompany it, and a mass of this mixed epithelial, lymphoid and spindle celled tissue frequently precedes in the thyroid the appearance of the internal parathyroid and may remain for some distance alongside it.

In

In those portions of the duct described as lined in part with ciliated epithelium it is difficult to be sure that the fringed appearance seen along the free end of the cells is due to actual cilia, or is a raggedness left by the shrinking away from the sides of the duct of the epithelial debris which is found in all the channels at some stage of their development or involution. The regularity of the fringe, however, in one or two instances is very suggestive of true cilia.

Certain features are common to the duct in all its forms.

(1) That the channels have origin in the breaking down of epithelial cells of a type quite distinct from those of the parathyroid and thyroid and easily recognisable in the midst

midst of either of these. The epithelial cells of the "duct" are larger than those of the thyroid or parathyroid, they stain as a rule, more faintly, and they are sometimes peculiarly clear and almost refractile in appearance.

(2) That there is associated always with the ducts at some stage of their course and frequently throughout the whole of their course, a greater or less amount of lymphoid tissue closely resembling thymus. Mixed with the round lymphoid cells are many spindle shaped cells such as have been described by Dudgeon[2] (Journal of Path.& Bact.1905, p. 173) as occurring in the thymus in atrophy.

(3) That they are almost always in some part of their course in close connection with one or other of the parathyroids.

(4) That they contain a large amount of homogeneous necrotic

necrotic material obviously derived from broken down epithelial cells, and differing as a rule, in its staining properties from the colloid of the thyroid vesicles.

(5) That they all appear to end blindly and must therefore be closed sacs - smaller or greater - and not ducts.

(6) That the tissue round about them is not specially vascular and that they do not seem to come into any very close relationship with blood vessels.

Thyroids of 11 dogs were examined in serial section, and a duct structure of precisely the same nature as that of the cat was found in all but three.

The

The "duct" in the thymus.

Seven thymus glands were examined, but in only 4 of these - 3 dogs and 1 cat - was the complete gland gone over in serial section. Portions only of the other 3 glands - 2 cats and 1 dog - were looked at.

In three of the glands, 2 dogs and 1 cat, in which a complete examination was made a duct structure similar in every way to that found in the thyroid and parathyroids was observed to be present.

In the other gland the Hassall's corpuscles were abnormal - very large and very numerous, many of them showing necrotic centres which in some cases had broken down and completely or partially disappeared leaving only the outermost layers of flattened epithelium bounding a lumen, clear sometimes and sometimes containing a certain amount of necrotic

necrotic epithelial debris; the whole structure bearing a strong resemblance to the duct in some of its phases.

In the three cases in which portions only of the gland were examined, the duct was not found.

The duct repeated in the thymus all the variations which it showed in the thyroid, parathyroids and thymic nodules round the thyroid. Tall columnar epithelial lining with a very definite basement membrane was however more frequently seen, and sometimes the lumen of the duct was filled with lymphocytes or the products of their degeneration rather than with epithelial cells.

It was seen most often in the fibrous stroma dividing the gland into lobules, Plate 5 (Fig.2), or in fibrous tissue towards the periphery of the gland, Plate 5 (Fig.1), but was also observed in one of the glands in the medullary portion

portion of a lobule, Plate 5 (Figs. 3, 4, 5. Small pieces of parathyroid tissue were sometimes seen in the neighbourhood of the duct, and were present, though not necessarily near the duct, in two out of the four thymus glands examined completely (1 dog and 1 cat). The most interesting feature of the duct as seen in the thymus was the fact that Harsall's corpuscles could be seen quite definitely to be budded off from the epithelium of its walls, and were observed frequently to be the termination of some of its loculi.

Several theories have been advanced as to the origin of Hassall's corpuscles.

Afanassieu[3] (1877, quoted by Goodall) held that they were blood vessels whose epithelium had proliferated, containing fused and degenerated blood.

Schambacher[4]

Schambacher[4] (1903 quoted by Goodall) interpreted them as arising from the presence or persistence of ducts in the thymus.

Goodall[5] (Journal of Physiol.1905) holds that they arise by the cutting off from their source of nutrition of masses of the original thymic epithelium by invading leucocytes. The masses thus cut off are said to degenerate and form concentric Hassall's corpuscles.

Moorhead[6] (Practitioner 1905) and Dudgeon (Journal of Path.& Bact. 1905) regard them as remnants of the epithelial structire from which the thymus gland was originally developed, and this appears to be the view most generally held at the present time.

Marine[7] ~~Warren~~ in a very recent paper, states that he considers that "normal Hassall's corpuscles represent the atrophic

atrophic and hyalinized remains of the embryological thymic epithelial tubules and cords" and bases his opinion upon the fact that one often finds in the one thymus gland all stages between well developed duct-like spaces, sometimes lined with ciliated epithelium, and fully developed Hassall's corpuscles.

My own series of sections fully bear out the view that Hassall's corpuscles are developed from this duct-like structure, but it has occurred to me that the "duct" is possibly the representative of a branchial cleft derivative other than the thymus or parathyroids, and that it may perhaps have some functional significance.

Mrs.F.D.Thompson[8], in a paper entitled The Thyroid and Parathyroid Glands Throughout Vertebrates - with Observations on some other closely related Structures - (Phil. Trans.

Trans.of the Royal Soc. of London, Series B. Vol.201) has described in elasmobranchs, Amphibia, frogs, reptiles and birds a "post branchial body" arising, according to Maurer, as an invagination of the ventral pharyngeal wall behind the 5th.gill cleft at the side of the aditus laryngis, and quickly separating off, remaining close under the epithelium. This body has been discovered in all craniata except cyclostomes and teleosts. It is described as consisting of three or four small vesicles lined with cylindrical epithelium, the cells of which sometimes carry cilia. The vesicles contain a coagulated albuminous substance and debris but no true colloid.

Mrs.Thompson describes the post branchial body in Chrysemys Picta as follows:- "it is in close relation to the parathyroid. It consists of a number of vesicles of varying size

size and shape though they tend to be spherical. The vesicles are of two distinct types, some large, with very low epithelium staining very deeply - others smaller, with cylindrical epithelium. Some of the vesicles contain a material which appears to be true colloid".

In birds the post branchial body is described as consisting of three parts - the first composed of compact epithelial cords, the second of spherical vesicles lined with cubical epithelium which may be ciliated, and the third of true parathyroid tissue and thymus.

In the pigeon - "the post branchial body has an extra-ordinarily complicated structure. It is obviously of epithelial origin and nature. It is composed largely of structures which at first sight resemble small arteries but whose walls are made up entirely of concentrically placed spindle

spindle shaped cells, and projecting into the lumen are irregular cells lining the tubules. The rest of the body appears to be built of structures identical with the various well known forms of Hassall's corpuscles of the thymus".

In the fowl - "the post branchial body is represented by a group of 8-10 vesicles lined with a low cubical epithelium, embedded in a constricted off portion of the elongated thymus. In the thymus nodule there is also a structure which must be put in the same category. This is a much infolded vesicle of large size lined with columnar ciliated epithelium".

It seems clear that the structures here described resemble very closely those I have found so constantly present in the thyroid, parathyroids and thymus of the dog and cat. That the Hassall's corpuscles are budded off from, or

or formed by a duct-like, tubular structure of some nature my sections demonstrate plainly, and it seems probable, considering the peculiar and varied forms taken by this structure and how nearly the description of the post branchial body given above applies to it, that we have in these parathyroid and thymus "ducts" and in the Hassall's corpuscles the representative of the post-branchial body.

The presence, almost invariably, in the duct loculi of quantities of necrotic - possibly colloidal material, obviously derived from the breaking down of epithelial cells, leads one to wonder whether the structure may not have some functional significance.

Also the cells with which the duct walls are lined have often all the characteristics of secreting cells.

Should it have a secretion it is probably of a different

different nature from that of the thyroid since (1) the cells from which the material filling the ducts is derived, are quite different from the rather small epithelium of the thyroid and parathyroid, and are easily distinguishable among them,- (2) the material filling the duct channels very often - though not always - stains differently from that filling the thyroid vesicles. In thymus nodes, and in the thymus itself the nature of the secretion may be different from elsewhere, since here we have often masses of lymphoid corpuscles filling the ducts, which break down sometimes like the epithelium and would therefore ~~constitute~~ contribute something to the secretion. Dudgeon[2] describes a cavity, sometimes containing a thick fluid, in the centre of each lobe, as a most conspicuous feature of large, or enlarged thymus glands in man. This fluid is found on examination to consist al-

most

almost entirely of degenerating lymphocytes, and its amount is so great as to give rise sometimes to the suspicion of abscess formation. Warthin[9] (Diseases of the Thymus - Osler and Macrae's System of Medicine 1915), holds that the so-called "abscesses of Dubois" found post-mortem in the thymus result from P.M. softening of the medullary portion of the thymus, and in other cases from the proliferation and subsequent degeneration of lymphoid cells in the corpuscles of Harsall.

It would seem possible that the thick pus-like fluid described as occurring in these "abscesses" is of the nature of a secretion and that the cavities are large duct loculi with their products of degenerated epithelial and lymphoid cells.

The presence of an identical structure in thyroid parathyroids and thymus is another indication of the extremely close

close relationship of these organs and may be one of the explanations of their apparent interdependence.

I desire to express my thanks to Professor Noel Paton for much kind assistance in the preparation of this paper.

References.

1 Pepere, Arch.Ital.de Biol.48 and 49.

2 Dudgeon, Journal of Path.& Bact. 1905, p.173.

3 Afanassieu, Arch.f.mikroscop.Anat.XIV. 1877.

4 Schambacher, Virchow's Arch.f.Path.Anat.v.Phys.CLXXII. 1903.

5 Goodall, Journal of Phys.1905, Post Natal Changes in Thymus.

6 Moorhead, Practitioner, Dec.1905.

7 Marine.

8 Mrs.F.D.Thompson, Phil.Trans.of the Royal Phil.Soc.of London, Series B. Vol.201.

9 Wurthin, Osler & Macrae's System of Medicine 1915. Diseases of the Thymus.

10. Paton & Findlay. Journal of Experimental Physiology Vol X No 3 & 4 1917.

SUMMARY

1. There is in the thyroid, parathyroid and thymus glands of cats and dogs a structure cyst-like in some of its forms, and duct-like in others.

2. In a series of 33 thyroids of cats examined in serial section this structure was found to be present in all. In 11 thyroids of dogs examined serially it was found in all but 3. In 4 thymus glands - 3 dogs and 1 cat - examined in serial section it was present in 3 - 2 dogs and 1 cat.

3. The lumen of the structure appears to be formed in the thyroid and parathyroids by the breaking down of large epithelial cells. Sometimes in the thymus it seems to be formed rather by the disintegration of lymphoid cells.

4. By the breaking down of these cells, epithelial and lymphoid, a

a homogeneous material is formed frequently filling the duct channels and loculi. This material stains pink sometimes with haemalum and eosin like the colloid of the thyroid vesicles, but more frequently takes a dark bluish black colour. It may perhaps be of the nature of a secretion.

5. The structure corresponds very closely in appearance with the "post branchial" body described in fowls and pigeons (and various lower animals) by Mrs.F.D.Thompson, and it is suggested that it may be the representative of this body.

6. Hassall's corpuscles can be definitely seen to be budded off from the epithelium forming the duct walls.

PLATE. I.

Fig. I.
(X 150)

Lymphoid & spindle celled tissue with patch of epithelial cells.

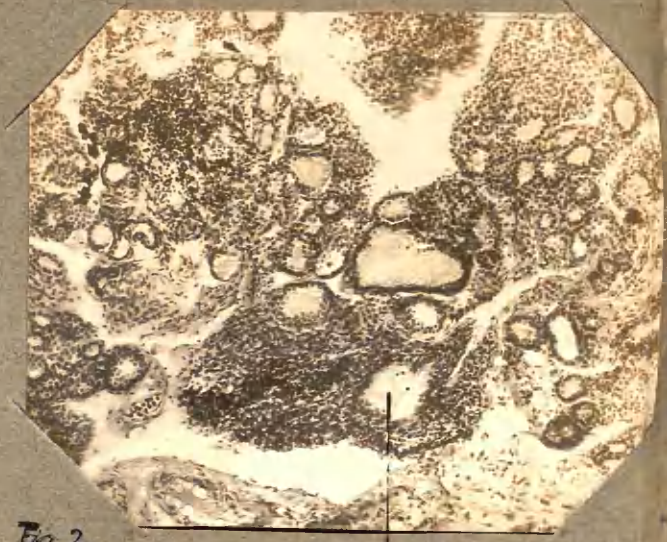
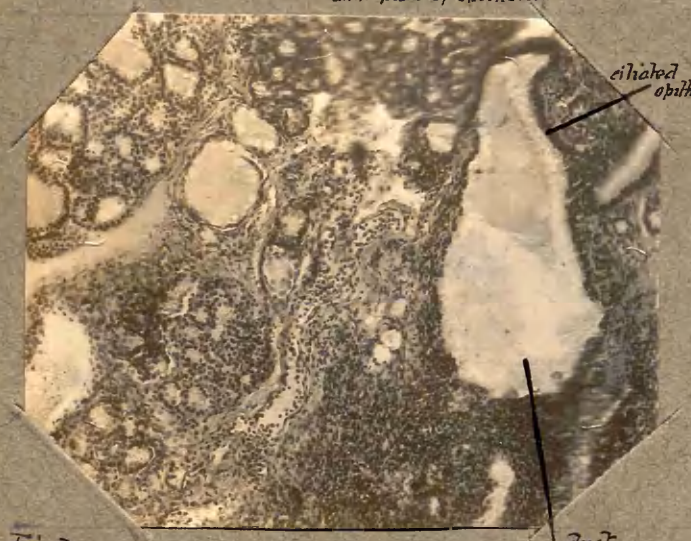


Fig. 2.
(X 150)

same patch as in Fig. I
Epithelial cells broken down forming duct.



ciliated epithelium.

duct

Fig. 3.
(X 150)

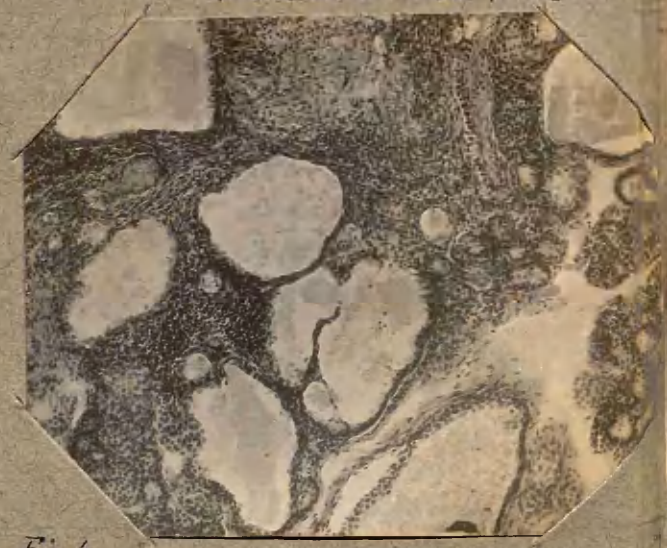


Fig. 4
(X 150)

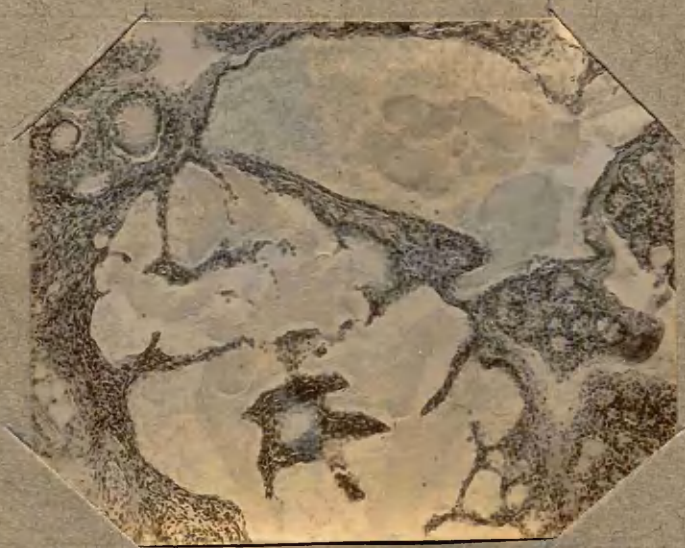


Fig 5.
(X 150)

PLATE 1.

Fig.1. Central portion of thyroid showing patch of lymphoid and spindle tissue containing epithelial cells.

Fig.2. Same patch as in Fig.1. Epithelial cells have broken down forming duct.

Fig.3. Later stage of duct, lined in part with ciliated epithelium.

Fig.4. Duct has become broken up into numerous loculi.

Fig.5. Very large thin walled duct loculi.

PLATE. 2.

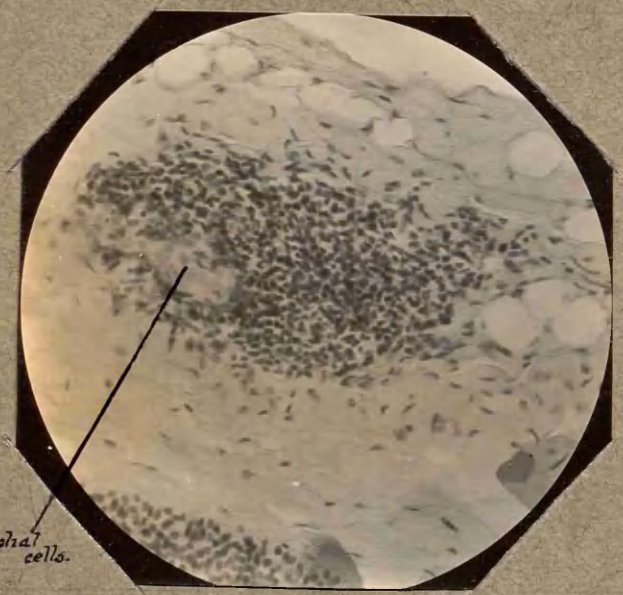


Fig. 1.
(X 350)

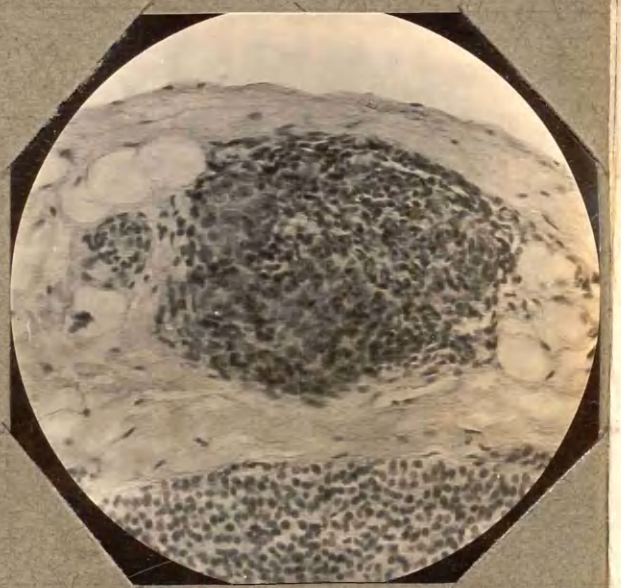


Fig. 2.
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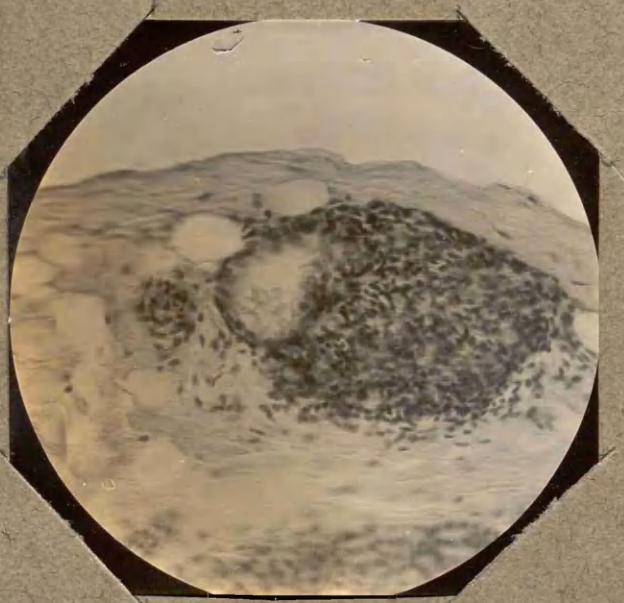

Fig. 3.
(X 350)

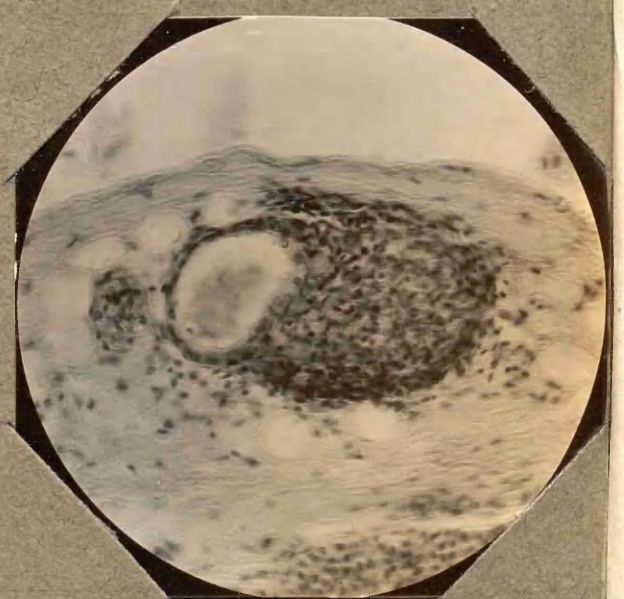

Fig. 4
(X 350.)

PLATE 2. To show development of duct in lymphoid nodule in capsule of thyroid, near external parathyroid.

Fig.1. Lymphoid node containing group of large clear epithelial cells.

Fig.2. Same as Fig.1, later stage.

Fig.3. Epithelial cells have broken down forming a duct channel.

Fig.4. Well defined duct channel containing some epithelial debris.

PLATE 3.

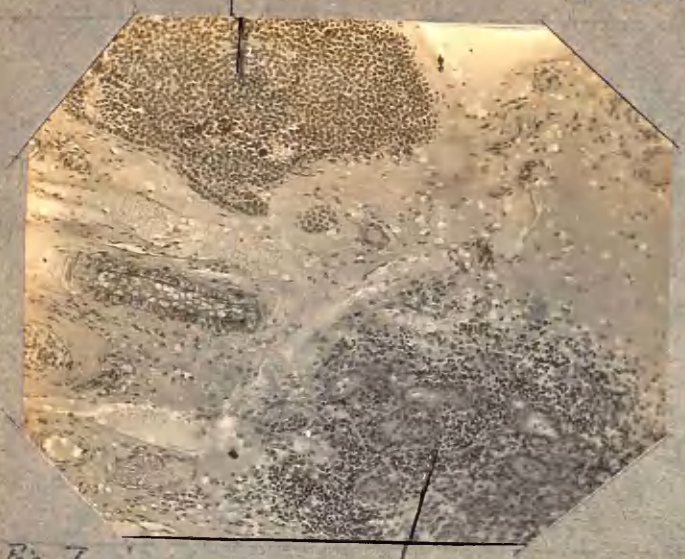

Fig. 1. (X 150)

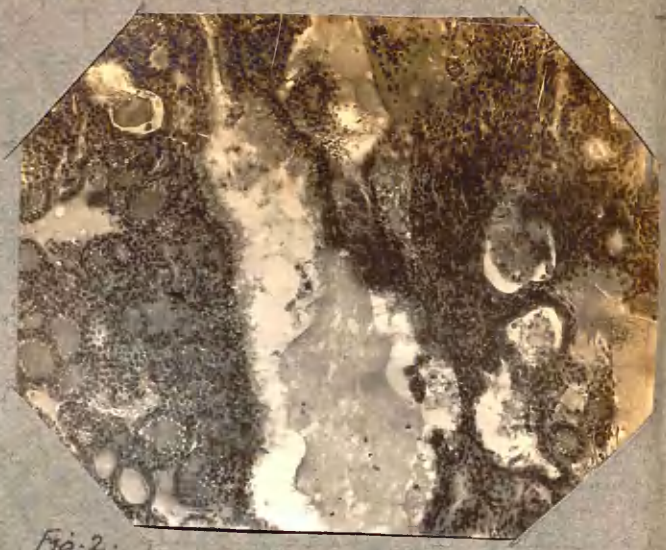

Fig. 2. (X 150)

Fig. 3. (X 150)

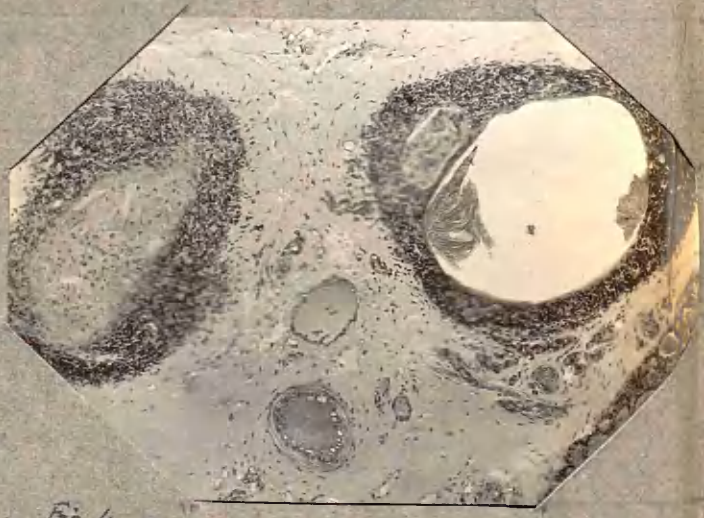

Fig. 4 (X 150)

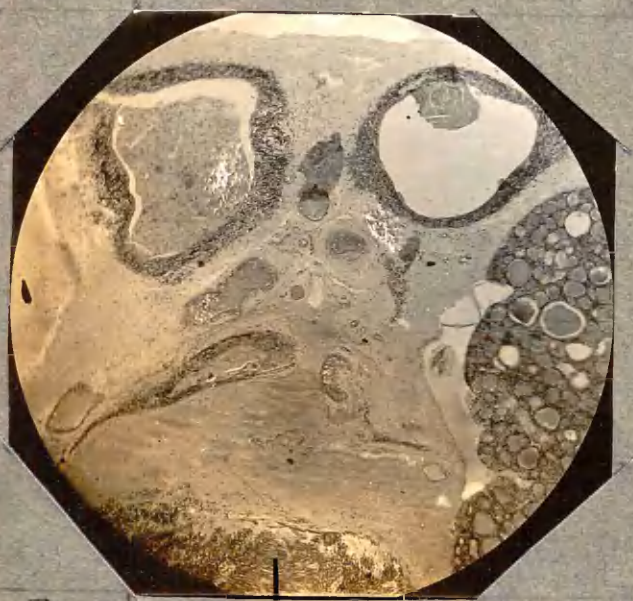

Fig. 5. (X 75)

Fig 6. (X 75)

PLATE 3.

Fig.1. Patch of lymphoid and spindle celled and epithelial tissue in centre of thyroid near internal parathyroid.

Fig.2. Large duct channel partially lined with columnar ciliated epithelium which has developed in patch of lymphoid tissue shown in Fig.1.

Figs.3 & 4. Duct channels developing in lymphoid nodes in capsule of thyroid by breaking down of epithelial cells.

Figs.5 & 6. Same as Figs.3 & 4 (later stage) to show relationship of nodes to external parathyroid.

PLATE. 4.

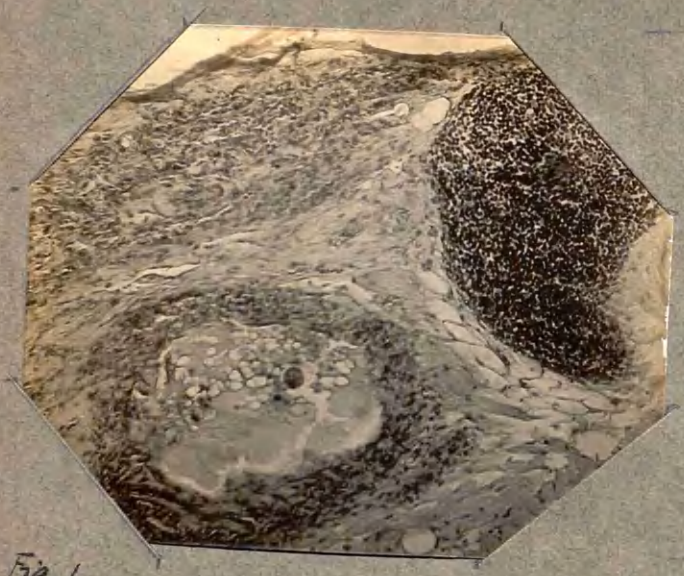

Fig. 1.
(X 150)

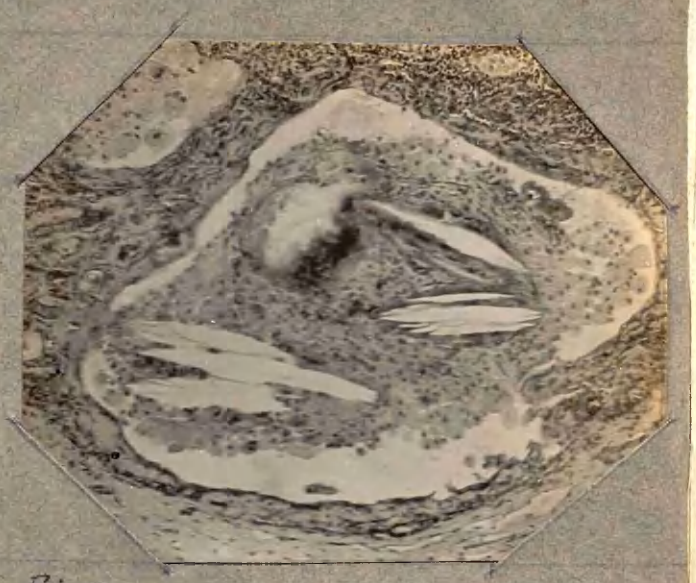

Fig. 2.
(X 150)

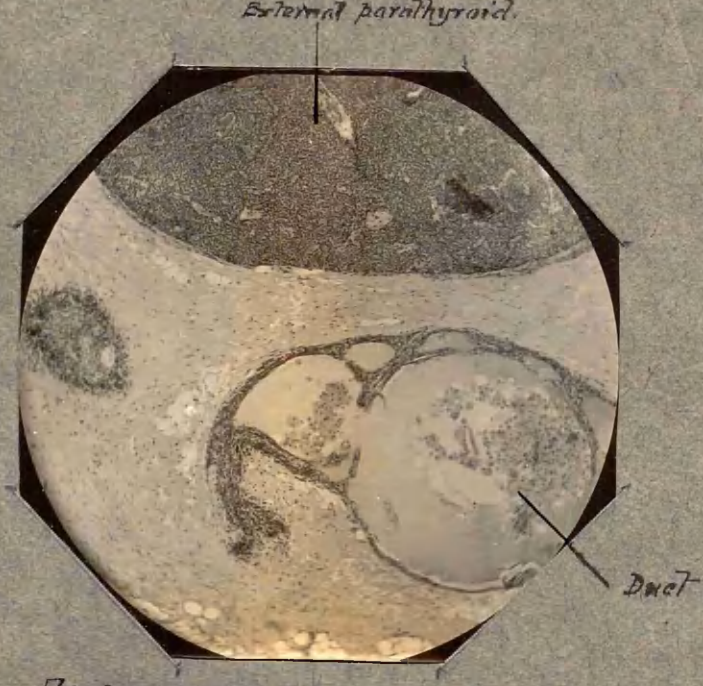

Fig. 3.
(X 75)

PLATE 4.

Fig.1. Duct channel in capsule of parathyroid containing degenerating epithelium.

Fig.2. Large duct channel in same situation as that in Fig.1. To show mass of degenerating epithelium with the peculiar longitudinal splits often observed in the masses contained in duct channels.

Fig.3. Large thin walled duct channel in same situation as Fig.1 and Fig.2, showing its position in regard to the external parathyroid.

PLATE. 5.

Duct in Thymus.

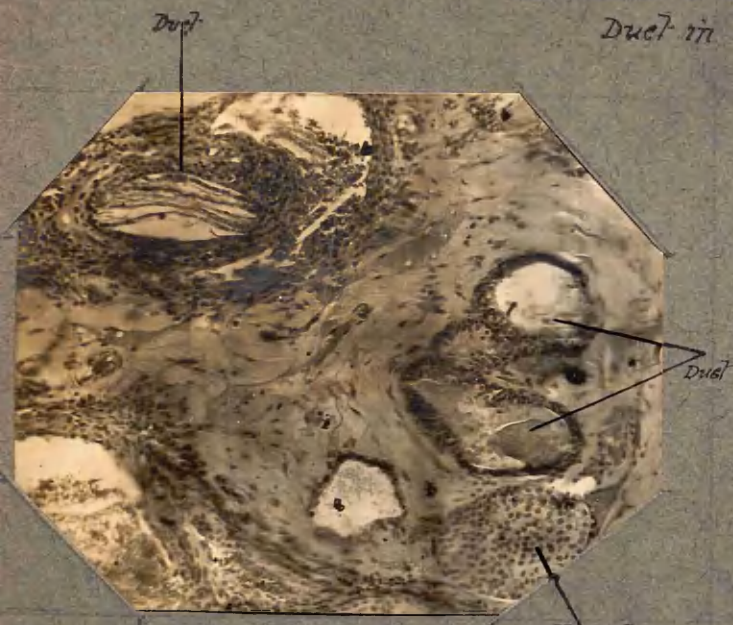

Fig. 1. (X 150)

Fig. 2. (X 150)

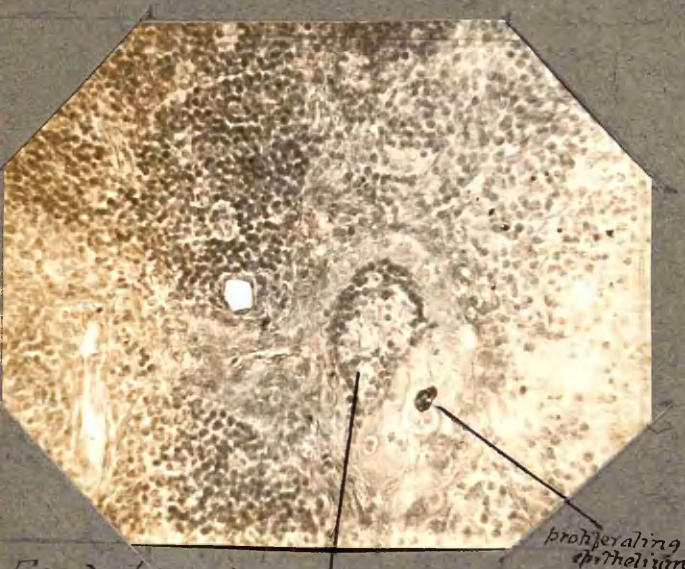

Fig. 3. (X 350)

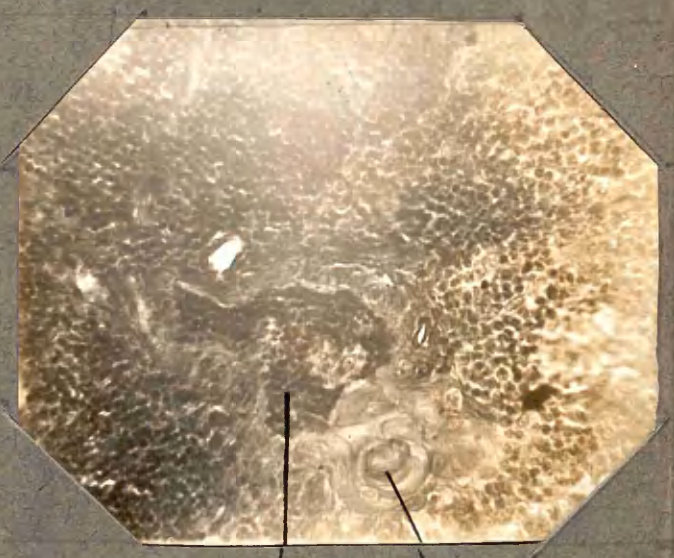

Fig. 4 (X 350.)

Plate 5. Duct in thymus.

Fig. 1. Duct in fibrous tissue capsule of thymus.

Fig. 2. Duct in centre of thymus lobule. Hassall's corpuscle forming at lower end.

Fig. 3. Duct in centre of thymus lobule. Proliferation of cells of wall. First stage of Hassall's corpuscle. Lymphocytes and epithelial cells in lumen of duct.

Fig. 4. Same as Fig.3. Second stage in formation of Hassall's corpuscle.

Fig. 5. Same as Figs.3 & 4. Hassall's corpuscle fully formed.